Remarks

Currently Claims 1-23, 25, 27-28 and 30-34 are pending. Claim 27 is amended herein to recite "human". It is respectfully submitted that the foregoing amendment raises no new issues and entry is therefore proper under 37 CFR 1.116.

Applicants acknowledge with appreciation the Examiner's allowance of claims 1-23, 25, and 32-34.

Section 112, First Paragraph Rejection Overcome

Claims 27, 28, 30 and 31 currently stand rejected under 35 U.S.C. §112, first paragraph, the Office Action stating that the specification, while enabling for treatment of prostate cancer, is not enabling for treating any or all proliferative conditions and any or all neoplasms based on the mode of action of the instant compounds as Plk inhibitors and mitosis inhibitors. Applicants respectfully maintain the traversal of the instant rejection. The analysis of the Wand's factors which was included in the prior response is not repeated here for the sake of brevity. Applicants respectfully maintain the points made in the prior response.

A specification that contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of 112, unless there is reason to doubt the objective truth of the statements contained therein. *In re Marzocchi*, 439 F.2d 220 (CCPA 1971). In the instant case, it is respectfully submitted that the Office Action has not met the burden of establishing a reason to doubt the objective truth of the asserted utility.

The outstanding rejection appears to indicate that the Examiner's doubt is really whether the claimed compounds would be effective in the claimed methods, not whether one skilled in the art would know how to administer a compound for the treatment of a neoplasm or how to contact a compound with a cell for purposes of inhibiting cellular proliferation or mitosis.

It is respectfully submitted that the how to use element of section 112, should not be used as a surrogate for the utility requirement. MPEP 2164.07

> Office personnel should not impose a 35 U.S.C. 112, first paragraph, rejection grounded on "lack of utility" basis unless a 35 U.S.C. 101 rejection is proper In particular, the factual showing needed to impose a rejection under 35 U.S.C. 101 must be provided if a 35 U.S.C. 112, first paragraph rejection is to be imposed on "lack of utility" grounds. MPEP 2161.07.

However, the claims have not been rejected for lack of utility and the Office Action has not provided the factual showing needed to impose a rejection under 35 U.S.C. 101.

Section 112 enablement does not require Applicants to prove safety, efficacy, etc of the claimed compounds. Section 112, requires Applicants to teach how such compounds can be used in the claimed methods–that is, how such compounds may be administered to a human in need thereof and how such compounds can be contacted with a cell.

Claims 30 and 31 recite methods for inhibiting proliferation of a cell and methods for inhibiting mitosis, respectively. Both methods recite the step of contacting the claimed compounds with a cell. Cellular proliferation assays are well known in the art and their use in identifying potential anti-tumor/anti-cancer agents is well accepted and routine. In addition to this general knowledge in the art, Applicants' specification, at pages 183-184, teaches specific assay methods for evaluating inhibition of Plk and inhibition of cellular proliferation, which methods comprise the step of contacting a compound of the invention to a cell. Thus, Applicants have expressly taught how to contact a compound of the invention to a cell for purposes of inhibiting proliferation of a cell or for inhibiting mitosis. The teaching of how to use the claimed compounds in this manner is commensurate with the scope of claims 30-31 --how to inhibit cellular proliferation or mitosis. One skilled in the art, based on this teaching can perform routine (high-throughput) experiments to evaluate the activity of any compound within the scope of the claims, in the same manner employed by Applicants. Thus, any experimentation to evaluate activity is routine in the art and therefore cannot constitute undue experimentation. *See*, *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988).

Claims 27 and 28 are directed toward methods for treating "a neoplasm susceptible to Plk". Claim 27 specifically recites the foregoing quoted language. Claim 28

depends from claim 27 and recites specific neoplasms. The literature clearly establishes that Plk inhibitors are known to inhibit proliferation of a cell and to inhibit mitosis. Inhibition of cellular proliferation is an accepted model for evaluating anti-tumor/anti-cancer activity. The Office Action does not provide a reasonable basis for one skilled in the art to doubt the accepted use of cellular proliferation as a model for anti-tumor/anti-cancer activities. Accordingly, the Office Action fails to provide a reason for a person of ordinary skill in the art to doubt that a compound which is known or shown to inhibit Plk and/or cellular proliferation will have utility in methods for treatment of neoplasms susceptible to Plk. In particular, the Office Action fails to provide reasons why one skilled in the art would doubt the objective truth of the asserted utility and enablement for those specific neoplasms recited in Claim 28.

With respect to the methods of treatment recited in claims 27-28, it is noted that:

> "[i]f a statement of utility in the specification contains within it a connotation of how to use, and/or the art recognizes that standard modes of administration are known and contemplated, 35 U.S.C. 112 is satisfied. *In re Johnson*, 127 USPQ 216, 219 (CCPA 1960); *In re Hitchings*, 144 USPQ 637, 643 (CCPA 1965), [and] *-n re Brana* 34 USPQ2d 1437, 1441 (Fed Cir 1993)." MPEP2164.01(c).

The specification provides ample support for Applicants' asserted utility. Applicants have taught methods (conducive to high-throughput screening) for evaluating Plk enzyme inhibition and inhibition of cellular proliferation in multiple tumor cell lines. Applicants have provided data for numerous compounds tested in several different tumor cell lines, including prostate cancer cell lines, colorectal tumor cell lines (Colo205, HCT116 and RKO), non-small cell lung cancer (NSCLC) cell line (H460), breast cancer cell lines (MCF7 and MDA435) and an osteosarcoma cell line (SAOS2). The data provided correlates to the asserted utility and is accepted in the art as a model for anti-tumor/anti-cancer activity. Applicants have taught how to administer the claimed compounds to an animal (e.g., human) in need thereof. Specifically, the disclosure describes how to formulate a compound of formula (I) into a pharmaceutical formulation and a variety of administration routes for achieving administration to an animal (e.g., human) (see, pages 36-41); which dosages should be administered (see, pages 32-33); and even methods for using the claimed compounds together with other therapeutic agents (see, pages 41-50). Regardless of the specific claimed compounds being used or the neoplasm being treated, the method of use that must be and has been taught is the same –administering the

compound to an animal in need thereof. Even if this teaching were not present, the specification would be enabling for how to use the claimed invention because one skilled in the art could obtain such information without undue experimentation since anti-cancer agents are known in the art. Thus, Applicants have in fact provided a teaching of how to use the claimed compounds which is commensurate with the scope of the subject matter sought to be patented by claims 27-28 and 30-31. In view of this teaching, Applicants respectfully submit that the Examiner has not met the burden of showing why one skilled in the art would reasonably doubt the asserted utility.

The Examiner acknowledges that the specification is enabling for treatment of prostate cancer (Office Action mailed 19 March 2008, page 2) and yet judges the disclosure to be insufficient for the treatment of other neoplasms susceptible to Plk, including those recited in claim 28. Given that the disclosure of how to use the compounds for treatment of a neoplasm susceptible to Plk is the same for all neoplasms within the scope of claims 27 and 28; and that cellular proliferation data in other tumor cell lines is provided in the specification; and that the method of using the invention is the same regardless of the neoplasm being treated or the compound employed; it is unclear how the specification can be enabling for prostate cancer and yet insufficient for treatment of, for example, colorectal cancer. The invention is used in exactly the same way for the treatment of all neoplasms susceptible to Plk. The compounds are used for treatment, according to the invention, by administering the compound to an animal (e.g., human) in need thereof and as shown above, Applicants' specification teaches how to use the claimed compounds for this purpose.

Applicants respectfully submit that the BPAI decision, *Ex Parte Eggenweiler et al.*, Appeal 2007-2495, decided 27 November 2007 (copy attached for the Examiner's convenience), supports Applicants' position. In *Eggenweiler*, the Board overturned an enablement rejection on facts which mirror the instant application. In that case, the Examiner rejected claims to methods of treating various conditions including "tumors" as failing to comply with the enablement requirement of section 112. Specifically, with regard to methods of treating tumors, the Examiner argued that the specification "does not provide sufficient information that all tumors are treatable by the herein claimed compounds described in the methods claimed."

The Board reiterated the well-established rule from *In re Marzocchi*, 439 F.2d 220 (CCPA 1971) that a specification that "contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of 112, unless there is reason to doubt the objective truth of the statements contained therein." *Eggenweiler*, *supra* page 3. The issue then, according to the Board, was not whether Appellants had established that the specification was enabling, but rather whether the Examiner had met the initial burden of setting forth a reasonable explanation of why it is not. *Id.*, at p.4. The Board summarized the Examiner's position as essentially that "[t]he nature of the invention is complex in that it encompasses the treatment of all types of tumors", there is no known anticancer agent which is effective against all cancers", and "practicing the invention would require "undue, unpredictable experimentation" "for each type of cancer." *Id.*

The Board held that the Examiner had not adequately explained why practicing the invention would have required undue experimentation because the reasoning was extremely generalized and did not address the inhibitory effects of the compounds, their antagonistic effects on the target or the role of the target in cancer. Secondly, the Board found that the fact that there is no known anticancer agent effective against all cancers is irrelevant. *Id.*, at p.5. Finally, the Board pointed out that there is no known authority, and none cited by the Examiner, that would require Appellants compounds to be effective against all cancers. *Id.*

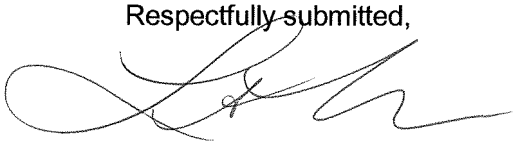
The same enablement rejection has been made in the instant case. *See*, page 5 of the outstanding Office Action: "[n]o compound has ever been found to treat diseases of all types generally," and page 14 of the prior Office Action: "it is beyond the skill of oncologists today to get an agent to be effective against cancers generally." The Board has held in *Eggenweiller* that this reasoning is insufficient to meet the PTO's burden of establishing lack of enablement.

In the instant case, the specification contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented, and as such it should be taken as in compliance with the enablement requirement of section 112.

As was the case in *Eggenweiller*, the Office Action fails to meet the burden of establishing a reason to doubt the objective truth of the statements contained in the specification. Withdrawal of this rejection is respectfully requested.

Applicants respectfully submit that the instant application is in condition for allowance, which action is respectfully requested. In the event that the Examiner maintains the rejection, an Advisory Action is respectfully requested prior to the due date for filing the Notice of Appeal (19 Jun 2008). The Examiner is invited to contact the undersigned at (919) 483-8222, to discuss this case, if desired.

Respectfully submitted,



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